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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	26

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/382,837	Borodic, G.E.
Examiner	**Art Unit**
G.R. Ewoldt, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *12/20/02 and 4/24/03* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19 and 21-23* is/are pending in the application.

4a) Of the above, claim(s) *9 and 13-16* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10-12, 17-19, and 21-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 22
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *petition decision*

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09/382837

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	26

DATE MAILED:

The decision on the petition filed in the above entitled application is as follows:

☐ Delay in Prosecution Held Unavoidable (35 U.S.C. 133),

Petition Granted _____

☐ Delayed Payment of Issue Fee Accepted (35 U.S.C. 151),

Petition Granted _____

☒ Petition Granted The petition filed 4/24/03 for acceptance of color photographs is hereby granted.

☐ Petition Denied _____

☐ Petition Dismissed _____

By direction of the Deputy
Assistant Commissioner for Patents

_____

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

DETAILED ACTION

1. Claims 1-8, 10-12, 17-19, and 21-23 are being acted upon.

2. Applicant's amendment and remarks, and the declaration of Dr. Martin Acquandro, filed 12/20/02, are acknowledged. Applicant's petition to accept color drawings, and three sets of said drawings, filed 4/24/03, are acknowledged.

3. Applicant's petition to accept color drawings has been granted.

4. The declaration stands objected to because it claims priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846 as indicated in the first line of the specification. A new declaration is required.

Applicant has again indicated that a new declaration will be submitted.

5. In view of Applicant's amendment and remarks all rejections under the second paragraph of 35 U.S.C. 112 have been withdrawn.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 17-19 and 21-23 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record as set forth in Papers No. 19, 13, and 11, mailed 8/26/02, 1/09/02, and 7/05/01, respectively. This is a new matter rejection.

Applicant's arguments, filed 12/20/02, have been fully considered but they are not persuasive. Applicant argues that the declaration of Dr. Martin Acquandro demonstrates "that one of ordinary skill in the art, when reading the specification as a whole as of the earliest priority date of the pending

application, August 25, 1998, would understand that the disclosure clearly describes the treatment of neurogenic inflammation and the anatagonism of at least one neurogenic mediator, and demonstrates that as of the earliest priority date of the pending application, August 25, 1998, the inventor was in possession of the invention as so claimed."

It is noted that Applicant's arguments as regard the rejection comprise reiterations of Dr. Acquandro's declaration. Accordingly, the declaration is herein considered and discussed.

The Declarant asserts that "One of ordinary skill in the art, as of the earliest priority date of the pending application, August 25, 1998, would understand that the invention encompasses a method of treating neurogenic inflammation when reading the "Summary of Invention" section of the application that discloses "this new bioeffect of anti-inflammatory action is explained by the resultant blockage of mast and nerve cell release of histamine and other preformed mediators which result in vascular dilation, increased permeability, altered sensory experience, edema and erythema." ("Summary of Invention", paragraph 3)." The Declarant continues "Additionally, one of ordinary skill in the art, as of the earliest priority date of the pending application, August 25, 1998, would understand that the invention encompasses the treatment of neurogenic inflammation and the anatagonism of at least one neurogenic mediator when reading the following disclosures: "[C]hemodegervative pharmaceuticals such as botulinum toxin...are effective anti-inflammatory agents" ("Summary of Invention", paragraph 2); "The subject anti-inflammatory agent's unique property relates to the suppression of the component for the inflammatory response which occurs rapidly, and which is mediated by neural reflex mechanisms" (Summary of Invention", paragraph 6)." The Declarant continues "The phrase "[I]flammation in torticollis in peripheral tissues may be neurogenically mediated".

In these three cites, the Declarant has quoted every disclosure of the terms "nerve", "neural", and "neurogenically mediated" disclosed in the specification. Said disclosures remain an insufficient written description of the invention as now claimed.

Regarding the disclosure of "nerve cell release of histamine", it is clear that histamine release by mast cells is the basis for the invention of the claims, "it has been found that low dosages of the subject chemodenervative agent reduces histamine releases and releases of other preformed mediators

associated with mast cell degranulation. The subject bioeffect is noted at low dosages of the chemodenervative agent in one animal model of ocular surface disease well noted for histamine release and releases of other preformed mediators associated with mast cell degranulation and rapid inflammatory response" (page 5). The single use of the term "nerve cell" is insufficient written description for the invention as now claimed.

Regarding "neural reflex mechanisms", the above mentioned cite is the only use of the term and this vague disclosure cannot support the invention as now claimed.

Regarding "neurogenically mediated" inflammation, as set forth in the previous Action, again note that the specification discloses that the inflammation of torticollis "*may*" be "neurogenically mediated". Clearly, at the time of filing, Applicant chose not to make a definitive statement regarding the nature of inflammation in even this single embodiment (torticollis). Thus, it cannot now be credibly argued that this minimal disclosure supports claims drawn to a method of treating all forms and embodiments of neurogenic inflammation.

The Declarant reiterates Applicant's previous argument that the instant specification is supported by the disclosure of the '768 patent, i.e., "the '768 patent shows the understanding that one of ordinary skill in the art would have during this time period."

It remains the Examiner's position that each application must be examined on its own merit. Each application must define its own claimed invention. The instant argument seems to imply that Applicant meant to claim the invention set forth in the '768 patent. Such an argument is not persuasive.

The Declarant continues this line of argument by asserting that several references of record, e.g., Sann et al. and McDonald et al., "disclose the understanding and meaning of neurogenic inflammation." Further, the Declarant asserts that the disclosure of a genus, e.g., "cytokines" or "preformed mediators", is sufficient to support the recitation of specific cytokines, e.g., interleukin-1 and interleukin-2 or preformed mediators, e.g., substance P.

Again, it is the Examiner's position that it is the specification and not the prior art that serves to define an invention. Additionally, even assuming *arguendo* that the specification could support the concept of "neurogenic

inflammation", there is no disclosure that can support *specific* mediators, such as those listed in Claim 19, nor *specific* diseases, such as gout (Claim 22). It is well established that the disclosure of a genus does not constitute the disclosure of the individual species within the genus.

It is also noted that neither the Declarant nor Applicant (in the remarks) has addressed the Examiner's previous point regarding the scope of the term "neurogenic inflammation", i.e., including interactions between the nervous system and keratinocytes, Langerhans cells, dermal microvasculature endothelial cells, infiltrating immune cells. As set forth previously, except for those with mast cells, these interactions are not disclosed in the specification, nor are many of the conditions/diseases that the method would now encompass treatments for. Accordingly, it remains the Examiner's position that the specification cannot support claims amended to recite a method of treating neurogenic inflammation.

8. Claims 2-4 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of reducing allergy induced conjunctivitis in a mouse comprising administering a botulinum toxin,

does not reasonably provide enablement for:

A) a method of reducing inflammation without causing muscle weakness,

B) a method of reducing inflammation comprising an effective dose of botulinum toxin less that 2.5 units,

for the reasons of record as set forth in Papers No. 19, 13, and 11, mailed 8/26/02, 1/09/02, and 7/05/01, respectively.

Applicant's arguments, filed 12/20/02, have been fully considered but they are not persuasive. Applicant asserts that "the specification provides a number of working examples of treating inflammation with a chemodenervative pharmaceutical, such as botulinum toxin, without causing muscle weakness, and with doses within the claimed range." Specifically, Applicant directs the Examiner to the example involving spasmodic torticollis.

Regarding "treating inflammation with a chemodenervative pharmaceutical, such as botulinum toxin, without causing muscle weakness", Applicant's assertion is factually incorrect. The specification simply does not disclose that said parameter (muscle weakness) was measured. Regarding the spasmodic torticollis example, it is noted that the example does not actually disclose that any specific dosage of any specific toxin

results in any specific outcome. Indeed, it is unclear whether the example is intended to disclose experimental results or merely representative results. Note the actual wording of the example "Botulinum toxin injected into red areas noted to be painful and thermally active in accordance with the subject invention has been demonstrated to block the erythema, pain, increased tenderness, and heat loss within the area consistent with the denervation diffusion potential for the given dose, as can be seen in Figures 8A and 8B, in which Figure 8A shows the red patch and Figure 8B shows a blanched area of blocked inflammation at the injection site. Minimum doses range between 0.6 units to 15 units and are far lower than that required to produce regional weakness" (underlining added by Examiner). Note the use of the somewhat vague phrase "has been demonstrated". There is no indication that said demonstration is actually in the form of an experiment performed as a working example for inclusion in the instant application. Indeed, the example never actually discloses that the procedure was performed nor that any specific dosing regimen was used. The employed wording could simply mean that the results of the figures might represent what would be expected to happen if the method of the claims was performed. Accordingly, this "example" cannot support the limitations of the claims. Additionally, there is no disclosure of the use of the specific range of "below 2.5 botulinum units" as claimed.

Applicant argues that the conjunctivitis example supports the limitations of the claims.

It remains the Examiner's position that the disclosure of a single dosage in a single example is insufficient to support a claim to a range of dosages for the treatment of any type of inflammation.

9. The instant application claims the benefit of priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846. Claims 1-8 and 10-12 are granted said benefit of priority. However, it remains the Examiner's position that the '846 application does not teach a method for treating neurogenic inflammation. Accordingly, Claims 17-19 and 21-23 are denied the benefit of priority. The priority date of said claims is the filing date of the instant application, 8/25/99.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 3c of this title before the invention thereof by the applicant for patent.

11. Claims 1, 5-6, and 17-23 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,063,768 (filed 9/04/97), for the reasons of record as set forth previously.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 5-8, 10-12, and 17-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,063,768 (filed 9/04/97)) in view of The Merck Manual (1992) for the reasons of record as set forth previously.

Applicant has requested that an interference be declared between the instant claims and the claims of the '768 patent.

14. No claim is allowed.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the

statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. **Please note**: any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 Customer Service Center at (703) 308-0198.

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
September 23, 2003